REMARKS

Claims 1-10 are pending in the instant application. Claims 9 and 10 have been withdrawn from consideration and canceled. Claims 1-8 have been rejected. Claim 1 has been amended and claim 2 has been canceled. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Election/Restriction

The restriction requirement placing the claims into Groups I and II has been deemed proper and made final. Claims 9 and 10 have been withdrawn from further consideration. Accordingly, Applicants are canceling claims 9 and 10 without prejudice, reserving the right to file continuing applications for the canceled subject matter.

II. Rejection of Claims Under 35 U.S.C. §112

Claims 1-8 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is suggested that it is unclear how Y_1 and Y_2 can contain from 0, 1, 2, or 3 nucleotides *and* independently contain a sequence with 4 nucleotides (SEQ ID NO:1). Applicants respectfully disagree with this rejection.

In an earnest effort to facilitate the prosecution of the instant application, Applicants have amended claim 1 to clarify that at least one of Y_1 or Y_2 is 4 to 8 nucleotides in length, wherein a Y_1 or Y_2 of at least 4 nucleotides comprises the sequence 5′-UUYG-3′/2′ (SEQ ID NO:1). Support for this amendment

is found in the passage at page 9, lines 9-15, which states that "at least one of Y_1 or Y_2 is a length of 2 to 8 nucleotides, preferably 4 nucleotides; and Y_1 or Y_2 each independently ... are of the sequence 5'UUYG'3'/2' (SEQ ID NO:1)." In light of this clarification, reconsideration and withdrawal of this rejection is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. §102 or §103

Claims 1-7 have been rejected under 35 U.S.C. 102(b) or 35 U.S.C. 103(a) as being anticipated by or obvious over Hannoush et al. (Document AE, PTO-1449 filed 10/4/04). The Examiner suggests that Hannoush et al. teach a compound comprising two complementary strands 4 nucleotides in length, wherein the strands can be RNA or DNA or both and further wherein the strands are linked by a 5',3'-linked loop identical 4 nucleotides in length comprising SEQ ID NO:1. It is suggested that the compound taught by Hannoush et al. meets the structural limitations of claims 1-7 and would be expected to inhibit the RNase H activity of a retroid virus reverse transcriptase.

Claims 1-5 have also been rejected under 35 U.S.C. 102(b) or 103(a) as being anticipated by or obvious over Wasner et al. (Document AM, PTO-1449 filed 10/4/04). It is suggested that Wasner et al. teach a compound comprising two complementary strands 18-23 nucleotides in length, wherein the strands can be RNA or DNA or both and further wherein the strands are 5',3'-linked or 2',5'-linked. It is suggested that the compound of Wasner et al. meets the structural limitations of claims 1-5 and would be expected to inhibit the RNase H activity of a retroid

virus reverse transcriptase. Applicants respectfully disagree with these rejections.

Hannoush et al. teach a single hairpin loop structure composed of DNA, RNA, or both. Wasner et al. teach DNA:DNA, RNA:RNA, RNA:DNA, RNA:2′,5′-RNA, and DNA:2′,5′-RNA duplexes lacking hairpin structures. In contrast, the instant invention is drawn to hairpin and dumbbell structures of Formula I with Y_1 and Y_2 composed of a ribonucleic acid; 2′,5′-linked ribonucleic acid; or combination thereof; and X_1 or X_2 comprised of an arabinonucleic acid; a 2′-fluoro-arabinonucleic acid; a locked nucleic acid; a 2′-fluoro-ribonucleic acid, a peptide nucleic acid; or a combination thereof. Accordingly, in an earnest effort to clarify the features of instant composition, Applicants have amended claim 1 to indicate that X_1 or X_2 are comprised of an arabinonucleic acid; a 2′-fluoro-arabinonucleic acid; a locked nucleic acid; a 2′-fluoro-ribonucleic acid; a peptide nucleic acid; or a combination thereof. Support for this amendment is found in claim 2 as filed and page 11, lines 4-7, which indicates that "when an inhibitory agent of Formula I contains an oligonucleotide strand (*i.e.*, X_1 and X_2) composed of RNA, said RNA may be substituted at the 2′-position by a fluorine". In light of this amendment, claim 2 has been canceled. Because Hannoush et al. and Wasner et al. fail to teach or suggest the claimed composition, these references fail to anticipate or make obvious the instant invention in accordance with MPEP 2131 and MPEP 2143. It is therefore respectfully requested that these rejections be withdrawn.

IV. Rejection of Claims Under 35 U.S.C. §103

Claims 1-8 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Andreola et al. (Document AA, PTO-1449 filed 10/4/04), in view of Park et al. (Document AJ, PTO-1449 filed 10/4/04) and further in view of Hannoush et al. (Document AE, PTO-1449 filed 10/4/04). It is suggested that Andreola et al. teach an oligonucleotide that is targeted to and inhibits the RNase H activity of a retroid virus reverse transcriptase. The Examiner acknowledges that Andreola et al. do not teach that the oligonucleotide comprises antiparallel complementary oligonucleotide strands that associate to form a duplex RNA or RNA and DNA and further are linked to a ribonucleotide having a sequence provided as SEQ ID NO:1. The Examiner suggests that Park et al. teach an oligonucleotide consisting of a sense and an antisense complementary region 22 nucleotides in length comprising RNA and DNA and further comprising two alkyl loop structures. It is suggested that Hannoush et al. teach a 2′,5′-linked ribonucleotide loop structure 4 nucleotide in length and identical to SEQ ID NO:1.

It is suggested that it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the oligonucleotide taught by Andreola et al. for the circular oligonucleotides taught by Park et al. to inhibit RNase H activity of a retroid virus reverse transcriptase and further obvious to substitute the loop structures of the circular oligonucleotide taught by Park et al. with the 2′,5′-linked RNA loops of Hannoush et al. The Examiner suggests that Park et al. motivates the use of circular oligonucleotides because they have increased resistant and cellular uptake. It is further suggested

that Hannoush et al. motivates the use of a tetraloop structure comprising the sequences provided as SEQ ID NO:1 because tetraloops are extremely stable and are important structural motifs for the design of synthetic nucleic acids. The Examiner suggests that one would have reasonable expectation of success because Park et al. teach that circular oligonucleotides show increased resistance and uptake into cells and further have greater inhibitory effects compared to antisense oligonucleotides. A reasonable expectation of success is further suggested because Hannoush et al. teach that a hairpin structure comprising a tetraloop is stable and the increased stability is seen with duplexes having RNA or RNA and DNA. Applicants respectfully traverse this rejection.

To establish a prima facie case of obviousness, three basic criteria must be met. *First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.* Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). MPEP 2142.

The oligonucleotides of Andreola et al. form G-quartets and bind to and inhibit the activity of RNase H. In contrast, the circular oligonucleotides of Park et al. impart an antisense effect. See page 959, column 1, second full paragraph, which

indicates that the circular oligonucleotides described therein are a new class of antisense oligonucleotides which efficiently bind to target mRNA. Accordingly, replacing the oligonucleotide of Andreola et al. with the circular oligonucleotide of Park et al. would render the oligonucleotide of Andreola et al. unsatisfactory for its intended use because the oligonucleotide of Park et al. imparts an antisense effect and the oligonucleotide of Andreola et al. is an inhibitory ligand. In making a modification to a prior art reference to arrive at the claimed invention, MPEP 2143.01 states that if the "proposed modification would render the prior art invention being modified unsatisfactory for its intended use, then there is no suggestion or motivation to make the proposed modification." Accordingly, there is simply no suggestion or motivation in the cited prior art references of Andreola et al. and Park et al. to make the proposed modification and further incorporate the tetraloop of Hannoush et al. Therefore these references fail to make obvious the instant invention in accord with MPEP 2142. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

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